EXHIBIT B

TVT Expert Report of Robert M. Rogers, Jr. M.D.

I. Qualifications

I am board certified in Obstetrics and Gynecology since 1986, and since 2013, also board certified in Female Pelvic Medicine and Reconstructive Surgery. Both of these board certifications are currently active. I presently have an active practice of gynecologic surgery and referral urogynecology in northwest Montana, in Kalispell, since the summer of 2005. I recently stepped down as the chief of the Department of Gynecology at the Kalispell Regional Medical Center.

I graduated from Princeton University in 1971 with an A.B. in Chemistry. I then worked for a pharmaceutical company, ALZA, in Palo Alto, California, as part of a team in developing transocular delivery systems for medications for glaucoma. In 1975, I began my medical studies at the University of Lausanne in Lausanne, Switzerland. After two years of study there, I transferred to my sophomore year at Temple University School of Medicine in the Fall of 1977.

I graduated from Temple University School of Medicine in 1980, and then, completed a four year residency in obstetrics and gynecology at The Reading Hospital and Medical Center in June, 1984. From there, I established a solo practice of general obstetrics and gynecology in Western Pennsylvania, in Kittanning at the Armstrong Memorial Hospital. In performing many reparative vaginal surgeries at that time and following up with my patients post-operatively, I realized that the 'traditional' ways of surgically repairing vaginal cystoceles, enteroceles, rectoceles, uterovaginal prolapse, and hypermobile urethra for stress urinary incontinence resulted in a high recurrence of these same vaginal support defects. The surgical results from these procedures, in my experience, had unacceptable failure rates.

After 6 ½ years of practice in Western Pennsylvania in January, 1991, I left Kittanning at the invitation of a group of obstetricians and gynecologists in eastern Pennsylvania in Reading at The Reading Hospital and joined them at The Women's Clinic, a private practice of 6 doctors. At this point in my career, I actively pursued my interest in the surgical anatomy of the female pelvis, and in the anatomy of urinary and fecal continence and vaginal support. In addition to much reading in textbooks and articles in the gynecologic and anatomic literature, I spent many hours performing cadaveric dissections in the medical student anatomy lab at the Jefferson Medical College in Philadelphia with the gracious permission of Dr. Richard Schmidt, professor of Anatomy and head of the medical student anatomy course and cadaver lab. As my studies and learning evolved, I began to lecture in various subjects in practical gynecologic surgical anatomy at the Reading Hospital, at the University of Pennsylvania department of Obstetrics and Gynecology, at Temple University, and other hospitals and departments of gynecology in eastern Pennsylvania, New Jersey and Maryland. Further, I taught anatomic and surgical instruction to OB/GYN residents from the Reading Hospital and Medical Center and the University of Pennsylvania from 1992 through 2005.

During the early 1990s, I began attending the scientific meetings of the Society of Gynecologic Surgeons. At these meetings, I gave several general session presentations on my anatomic work in gynecologic surgery. In 1995, I was elected to membership. As the result of my association with the Society of Gynecologic Surgeons, I met Drs. Cullen Richardson and Sandra Retzky, both actively involved in the study of female pelvic and vaginal support anatomy. In the summers of 1993 and 1994, we three and Dr. Gene Colburn, a professor of Anatomy at the Medical College of Georgia, spent 3 full days each year in the cadaver dissection lab at Rush Medical College in a pursuit of intense learning. These days were important for all of us in understanding the anatomy of pelvic and vaginal support and the anatomy of urinary and fecal continence. These sessions in conjunction with the anatomic work of Dr. John DeLancey at the University of Michigan produced several chapters and publications on these subjects, which helped to establish the current and accepted anatomic framework used in reconstructive vaginal surgeries performed today. In 1995, Dr. Sandra Retzky and myself wrote a *Ciba Clinical Symposia* (Vol. 47, No. 3, 1995), "Urinary Incontinence in Women." This booklet was one of the first publications with illustrations and explanations of our current knowledge of pelvic and vaginal support anatomy.

At the same time in the middle 1990s, I was invited to Baltimore by Drs. Al Bent, Geoff Cundiff and Harry Johnson, all practicing reparative vaginal surgeons and urogynecologists. Dr. Johnson had the insight to gather laparoscopic instrumentation and unembalmed human cadavers for important and ground breaking anatomic studies. We, together, began to perform laparoscopic surgical dissections at the Maryland Anatomy Board in the basement of the University Of Maryland School Of Medicine. These several sessions of anatomic dissections on unembalmed cadavers, as opposed to the stiffer embalmed bodies we had previously used, opened up a whole new way of learning and teaching surgical anatomy and surgical dissection techniques, which has become a present day standard of surgical teaching and learning in many surgical specialties. We held our first surgical course of anatomic teaching from unembalmed cadavers in Florida in October, 1996. Since then, I have been the program chair for many open, vaginal, laparoscopic and robotic anatomy courses using unembalmed cadavers (please refer to my CV).

Because of my experience in reconstructive/reparative vaginal surgery and my concerns with my failure rates, and those reported in the literature, I began to talk with my colleagues at the meetings of the Society of Gynecologic Surgeons and the AAGL. The AAGL is the largest organization in the world of gynecologic surgeons. This organization emphasizes the study and teaching of minimally invasive gynecologic procedures, such as those performed per vaginum, with the laparoscope, and with the da Vinci robot. In the late 1990s and early 2000s, I spoke with Dr. Tom Julian, Professor of Gynecology at the University of Wisconsin. During our discussions, he mentioned that he was beginning to use a sheet of polypropylene mesh placed in the anterior vaginal compartment in order to increase his success rate of anterior vaginal wall prolapse repair (cystocele repair). He verbally reported to me a very impressive success rate. I was, of course intrigued, and began to investigate the use of mesh in the vagina. He told me, to paraphrase his words, that he would tolerate a 7% mesh erosion rate in order to achieve an almost 100% success rate in repairing patients sent to him with severe cystoceles and recurrent severe

cystoceles. He, of course, thoroughly counseled his patients, and they were accepting, as he reported to me.

Because of my expertise in understanding, teaching and performing anatomic dissections on unembalmed cadavers, I was invited by Ethicon to come to New Brunswick, New Jersey to teach vaginal support anatomy and to interact and consult with the research scientists and biomedical engineers in studying new possibilities for products to be used in surgery for repair of vaginal prolapse.

Since the early 1990s to the present, I have had the opportunity to teach various groups of gynecologic surgeons all over the United States and other countries of the world, including Austria, France, Belgium, Canada, South Korea, Japan and Australia. I have organized and taught unembalmed cadaver courses for teaching gynecologic surgical anatomy and surgical dissection techniques for various individual hospitals and academic departments of Gynecology, at various courses for gynecologic surgeons, for Ethicon and for Cook Medical, as well as for large professional organizations of gynecologic surgeons such as the Society of Gynecologic Surgeons, the AAGL, and The Society of Pelvic Reconstructive Surgery. I have had multiple opportunities to lecture with the thought-leaders in this country and in the world in pelvic/vaginal support anatomy and the various reconstructive surgeries, including use of the various Ethicon mesh products.

In the summer of 2005, my wife and I decided to have a change in our lifestyle and move from the East Coast to the West, in order to take advantage of more outdoor recreational activities. I met my present partner, Dr. Richard Taylor, through a mutual friend at the large AAGL Annual Meeting in 2004. Eventually, I did relocate my practice to northwest Montana to Kalispell.

Since I moved to Kalispell, Montana in the summer of 2005, I have established an active practice of gynecologic surgery and urogynecology, with more of my patient referrals and surgery involved with vaginal prolapse repairs and surgery for stress urinary incontinence and fecal incontinence. Since May of 2008, when our office converted to an electronic medical documentation system, I have performed over 700 surgeries, approximately 100 per year, for reconstruction of various vaginal support defects, with several hundred of these cases involved with placement of Gynemesh PS and the Prolift products from Ethicon for support of the anterior, apical or posterior segments of the vagina. I have performed over 200 midurethral slings on these patients, most of them involving the suprapubic midurethral TVT, TVT-O and TVT-Secur products from Ethicon. I have used both mechanically cut and laser cut TVT meshes and have not detected any clinical difference between the two in my clinical experience or in my review of the medical literature.

I am a member of the American College of Obstetricians and Gynecologists (ACOG), the American Association of Gynecologic Laparoscopists (AAGL), the Society of Pelvic Reconstructive Surgeons (SPRS – dissolved in 2012), and the Society of Gynecologic Surgeons (SGS). In addition to my leadership positions as a member of the Board of Trustees for the AAGL, Board of Trustees and Chairman of the Board for the Society of Pelvic Reconstructive Surgery, Education Committee member for the SGS, and Co-Chair of

the Video Review Committee for AAGL, I also serve as a peer reviewer for the Journal of Minimally Invasive Gynecology.

I have published extensively on the conditions and operative anatomy related to urinary incontinence and pelvic organ prolapse, the surgical treatment and complications related to both conditions, as well as training, teaching, and evaluating gynecologic surgeons.

During my career, beginning with my Ob/Gyn residency in 1980, I have performed different surgeries for stress urinary incontinence -- vaginal plication of the pubourethral fascia underneath the urethra; anterior colporrhaphy; needle bladder neck suspensions, such as Stamey; open and laparoscopic Burch procedures; open MMK; pubovaginal slings with biologic grafts; and midurethral synthetic slings, such as TVT retropubic, TVT-O and TVT-Secur from Ethicon. I have performed hundreds of each of these procedures.

Furthermore, during my career, I have performed thousands of surgeries for pelvic organ prolapse, including anterior colporrhaphy, posterior colporrhaphy, enterocele repairs, sacrospinous ligament colpopexy, uterosacral ligament colpopexy, and iliococcygeus colpopexy; bilateral paravaginal defect repairs per vaginum, open incision into the retropubic space of Retzius, with the laparoscope and with the da Vinci robot -- using the patient's own native connective tissues and with mesh products (Gynemesh PS, Prolift) and with biologic graft materials (Pelvicol, Biodesign/Surgisis). I have used the Gynemesh PS and Prolift mesh products several hundred times in my patients and have had great results. As with all surgeons' experiences, I have had occasional complications intraoperatively (for example, bleeding, or bladder or rectal entry); however, these intraoperative events were recognized and repaired by myself or with surgical consultation. These patients recovered well. Latent complications of urinary voiding dysfunction, postoperative pain or mesh erosion were handled individually depending on the patient's presentation and complaint. These postoperative problems and complications were well within those reported at professional conferences, discussions with my colleagues and in literature articles that I have read during my career.

In summary, over 90% of my own patients are pleased with the long-term results of their reparative vaginal surgeries using the Gynemesh PS and Prolift products. They are comfortable without any vaginal or pelvic pressure, vaginal intercourse is comfortable, especially with use of vaginal estrogen cream and appropriate personal lubricants. They can urinate and empty their bladders and leak none to very little urine with physical stress maneuvers. Their bowel movements are soft and regular and are passed completely without straining. The vast majority when asked are very happy they decided to have their surgery. I see some of these patients because they return to see me with concerns about the lawyers' television advertisements about vaginal meshes. After taking a updated history and performing a physical exam, I am able to further reassure these patients, and of course, they are relieved and pleased with the surgical results. They admit that their quality of life has improved. My professional experience with polypropylene meshes is confirmed by the gyn and urogyn literature. (Svabik et al., ISUOG, 2014; Altman et al., NEJM, 2011; Jacquetin, Int Urogynecol J, 2013)

I attended the TVT National Prof Ed training sponsored by Ethicon on February 1, 1999 with Dr. Vincent Lucente at Lehigh Valley Hospital in Pennsylvania. This training was comprehensive and very adequate for me to perform the TVT on my own patients safely. Dr. Lucente is an excellent instructor and was always available by phone to answer any of my concerns.

In addition to teaching and lecturing residents, fellows, and colleagues, I also consulted with Ethicon as a Professional Education Preceptor. From 2003 to 2007, I taught a variety of Ethicon courses, such as preceptorships, proctorships, telesurgeries, cadaver labs, and advanced users forums, on products such as the TVT-O, TVT-Secur, Gynemesh PS, and Prolift. I was part of the initial group that went over to learn the TVT-O procedure from Dr. de Leval, and shortly thereafter performed the second TVT-O in the United States.

From the late 1990s to 2007, I was asked by the research and clinical scientists at Ethicon to consult with them on the design and performance of the Prolift, TVT-O, TVT-Secur products, as well as one or two other developing products. I was asked to perform cadaver dissections to be sure that proper surgical dissection techniques would allow proper and safe placement of the various polypropylene mesh products. I was also involved in developing teaching methods for instruction of other pelvic and vaginal surgeons on why and how to use these mesh products, the pelvic anatomy, the properties of the mesh, and the safe and effective use of the products. Ethicon engineers and medical directors also asked for my clinical input and opinions of these products. I found that at Ethicon all my contacts, discussions and work with the research scientists, biomedical engineers and clinicians were consistently respectful, appreciated, and honest. The work environment attitude was always one of 'How can we best help the patient with this problem and eliminate any and all possible risks and potential complications.' I never felt pressure to push a product out. All the product development in which I was involved was thoroughly evaluated and reevaluated step by step, in accordance to the Ethicon standards, the industry standards, and of course, the FDA and federal government standards. There was no room for 'fudging' or manipulating data.

In the fall of 2003, myself, Dr. Vince Lucente, Gyn surgeon from Allentown, Pennsylvania, and the product leader from Ethicon, Mr. Brian Luscombe, traveled to France and Belgium. [Eth.Mesh.11543627]. In France, we observed Dr. Jacquetin, and then, Dr. Michel Cosson surgically place their version of the hand-fashioned Gynemesh PS product that eventually developed into the Prolift system of repair for vaginal prolapse. We asked the Prolift inventors many questions, looked at their data and observed their surgical techniques. They were very open and honest and frank. As the result of the French experience with native tissue vaginal repairs and their failures, we were told 9 French vaginal surgeons from all over France (the French TVM Group) had been brainstorming and working in close collaboration to develop better techniques for improving postoperative success rates in reconstructive vaginal surgeries. The use of mesh arms to anchor the polypropylene mesh laterally and apically in the pelvis was discovered by the group of 9 French surgeons to be the most secure and safest way to safely ensure better and more durable surgical results. A significant amount of work was done in France and at Ethicon in New Jersey to improve the

instrumentation for mesh placement and to establish the best way to place without tension the mesh, the mesh arms and the vaginal and surrounding tissues and organs.

Additionally, in Belgium, we observed Dr. Jean de Leval, the urologist in Liege who developed the TVT-O, perform several of these procedures on his patients with a hypermobile urethra and stress urinary incontinence. Again, we asked many questions and reviewed his unpublished data and clinical experiences. He and his colleagues were open and honest, as well as collegial. Dr. de Leval after lunch asked me to perform a cadaveric dissection for his team. I was pleased to do so, and performed the dissection to demonstrate the vascular and neuroanatomy on the outer portion of the obturator membrane. This dissection convinced me to perform the transobturator sling from 'inside to out' from the vagina. From this dissection, Dr. de Leval published a paper on the anatomy of the TVT-O procedure.

Upon returning to Ethicon in New Jersey, the development of the Prolift products and TVT products continued in earnest with the patients' best interests always at the top of each agenda. The professional education development was always evolving to best teach surgeons on the safe and effective use of Ethicon's products, on how to competently learn these new procedures, from the printed IFU to lecture presentations to unembalmed cadaver labs. The effort was sincere and thorough. During our lectures and presentations, we always took time to answer questions from the surgeons - whether from the lecture or from individual concerns from their own surgeries with or without the use of any mesh. Surgeons began to come to know Ethicon as a place to go for pelvic anatomy and surgical teaching and training. Didactic slides, discussions, and interactions with the training surgeons involved a discussion of the more common risks associated with the use of the device and generally how to manage common complications.

From my residency training and throughout my career, I have continually learned all about surgical risks and complications. From reading textbooks on gynecologic surgery, such as Te Linde's, and lectures and literature articles, as well as my own surgical experiences and multiple discussions at our Gyn section meetings, I am always thinking of ways to avoid surgical and treatment complications and how to best serve my patients. The development of a surgeon and his or her surgical techniques and improved procedures is an active, continuing process throughout his or her career. Any surgeon who operates will have surgical challenges and have to deal with the occasional complication - intraoperatively and/or postoperatively. As I teach to surgical residents, fellows and practicing surgeons, they will have to deal with surgical risks and complications their entire careers. The vast majority of these are not the result of poor surgical practice. They are the result of patient anatomic variation, or patient response to scarring, or unusually fragile tissues in the field of dissection, or unexpected pathology or medical condition. Pelvic and vaginal surgeons work very closely to the bladder and rectum and work with connective tissue filled with small blood vessels and visceral nerves. The reparative vaginal surgeon must have a three-dimensional working knowledge of a difficult to understand anatomy and use meticulous dissection techniques. This is a challenge for us teachers who teach to teach our colleagues.

Regardless of whether or not certain risks are listed in a manufacturer's IFU, residents, fellows, and surgeons are expected to be familiar with the well-known complications of gynecologic surgeries, with and without the use of mesh or graft materials. Likewise, residents, fellows, and pelvic floor surgeons are expected to review the medical literature and be aware of the frequency and severity of the complications for the procedures they perform. Similarly, medical students, residents, fellows, and surgeons do not rely on IFUs to learn about the risks and the frequency and severity of complications associated with native tissue repairs, such as anterior/posterior colporrhaphies or sacrospinous ligament fixations, as these procedures are not accompanied with an IFU. Residents, fellows, and pelvic floor surgeons are expected to be familiar with mesh properties, such as pore size and tensile strength, as well as complications associated with foreign bodies, such as vaginal mesh repairs or abdominal sacralcolpopexies.

II. Materials Reviewed

This report contains a summary of my qualifications, education, training, and experience, as well as my opinions based on my education, training, clinical experience, lectures, editorial experience, ongoing review of the medical literature, experience teaching other residents, fellows, and surgeons about surgical procedures, anatomy, and complications, as well as my discussions with colleagues, attendance at various professional society and continuing medical education events, and other materials and literature I have reviewed that are referenced in my reliance list. Such materials include, but are not limited to, the product IFUs, patient brochures, professional education slides, DVDs, and Surgeon's Resource Monograph, as well as internal company design documents, and plaintiffs' expert reports and the reliance materials referenced in the body of those reports. All of my opinions are held to a reasonable degree of medical and scientific certainty. I reserve the right to supplement my report if I receive additional information after signing this report.

III. Fees and Expert Testimony

Chart reviews, writing expert reports, phone consultations: $500 per hour
Face-to-face meetings with lawyers for deposition and trial preparations:
$750 per hour
Attendance at Depositions in Kalispell, Montana: $1000 first hour,
Thereafter -- $ 750 per hour

Deposition Attendance outside of Kalispell, Montana
and Trial Attendance: $6000 per day
Plus travel expenses

I have provided expert testimony in the following cases within the last four years:

- *Craigg vs. Harris-Stansil* (Superior Court of California, County of San Joaquin)
- *Vicari vs. Schwartz* (New Jersey)
- *Quincy vs. Teel* (Northern California)

Stress Urinary Incontinence Background (Portions taken from Ford 2015 Cochrane Review):

Stress urinary incontinence (involuntary leakage of urine on effort or exertion; or on sneezing, coughing or laughing) is the commonest form of incontinence in women and leads to a reduction in their quality of life. Women with stress urinary incontinence can also have problems with sexual intercourse, as leakage of urine can occur. One in three women over the age of 18 years will be affected by stress urinary incontinence at some point in her lifetime, and about 14% will have incontinence bothersome and severe enough to undergo surgery in their lifetime. [Ford 2015, Wu 2014]. Surgery is more effective than non-surgical options, such as pelvic floor physical therapy. [Labrie 2012].

Stress urinary incontinence "is associated with significant physical morbidity, sexual dysfunction, loss of independence and a reduction in psychological well-being, with consequent decreased participation in social and domestic activities (Wetle 1995; Thom 1998; Van Oyen 2002; Salonia 2004; Botlero 2010)." [Ford 2015].

Overall the prevalence of urinary incontinence in adult women has been estimated to be between 10% and 40%, and is considered severe in about 3% to 17%, with annual incidence ranging from 2% to 11% (Hunskaar 2002; Milsom 2009). The prevalence of SUI in women is between 12% to 46% (Irwin 2006; Botlero 2008; Coyne 2009). This is a potentially debilitating social problem with significant cost implications to the individuals and the healthcare service. The estimated annual cost to the healthcare system in the UK exceeds GBP 700 million and in the USA it is over USD 20 billion (Fantl 1996; Hu 2004; Turner 2004). There is also significant cost borne by women on an individual basis, with estimates of more than GBP 178 million annually (Turner 2004; Papanicolaou 2005). [Ford 2015].

Over the years, surgery to stop this problem has become less invasive, and there are many different types of operations available. Midurethral sling operations are commonly undertaken to try and cure stress urinary incontinence. These operations are suitable for women who are having their first operation to prevent incontinence, and also women who have had unsuccessful surgery previously. In a midurethral sling operation a tape is placed underneath the urethra, which is the tube that carries urine out of the bladder. When the woman coughs, the tape compresses the tube, thus providing the support necessary to prevent urine leakage. [Ford 2015].

There are different forms of urinary incontinence of which SUI is the most common type, accounting for at least 50% of cases of urinary incontinence in women (Hannestad 2000). SUI is the involuntary loss of urine that occurs with physical exertion (e.g. sporting

activities), or on sneezing or coughing (Haylen 2010). Urodynamic stress incontinence (USI) is the involuntary leakage of urine observed during filling cystometry, it is associated with increased intra-abdominal pressure, in the absence of a detrusor contraction (Haylen 2010). Two mechanisms for stress incontinence are recognized: hyper-mobility or significant displacement of the urethra and bladder neck during exertion, and intrinsic urethral sphincter deficiency (Blaivas 1988). These mechanisms may coexist in women (O'Donnell 1994).

Urgency urinary incontinence (UUI) is a sudden, compelling desire to pass urine, which is difficult to defer (urgency), accompanied by the involuntary loss of urine. Detrusor overactivity (DO) is a diagnosis that denotes involuntary detrusor contractions observed during the filling phase of a urodynamic assessment. It may be spontaneous or provoked and can be qualified according to cause - neurogenic or idiopathic (Haylen 2010).

Surgical Options:

In 1996, Black published a systematic review on the quality of studies evaluating surgery for stress urinary incontinence , the effectiveness of different procedures, as well as the frequency of complications associated with each procedure. [Black 1996, British Journal of Urology]. Black's systematic review, in a "pre-TVT" era, concluded that "There is an urgent need for some large, rigorous, prospective studies of high quality. Until such studies have been completed, recommendations as to the best clinical practice cannot be based on scientific evidence." Black described how a wide variety of procedures had been developed to treat SUI, including "colposuspension, anterior colporrhaphy, needle suspension and sling procedures." At the time of the review, which consisted of a Medline search from 1966 to 1995, an Embase search from 1980 to 1995, and various other searches, the results returned a total of only 11 RCTs. In the short life span of TVT, there are well over 100 RCTs evaluating the safety and efficacy of the device.

Burch Colposuspension:

The Burch Colposuspension procedure is a highly invasive procedure with increased morbidity and lower cure rates compared to TVT and synthetic midurethral slings. A significant number of the clinical studies evaluating the Burch colposuspension were published at a time when scientific rigor was not as predominant as it is in the midurethral sling era, and many of the Burch studies were based on small case series with loose definitions for success, short follow-up periods, and low patient follow-up rates. In 1995, Alcalay described a time-dependent decline with Burch at 10-12 years with a plateau of a 69% cure rate. Out of the 366 women who were invited to follow-up, "161 did not reply or had difficulty attending, 71 had changed address and could not be traced, and 25 had died." Alcalay also found a significant decrease in objective cure for women who had undergone previous continence surgery. Alacalay also discussed how "Voiding difficulty is a recogni[z]ed complication after colposuspension," noting 22% of patients who still complained of voiding difficulty at +10 year follow-up. In addition, a 14 year Burch follow-

up study reported only 19% of women who remained completely dry, and 56% of women demonstrated significant leaker (i.e., failure) at 14 year follow-up. [Kjolhede 2005]. Similarly, the SISTEr trial reported a 7 year decline in cure rates down to 27% for the autologous sling group and 13% for the Burch group, with a corresponding decrease in patient satisfaction. [Richter 2011].

Langer (2001) reported post-operative Burch complications, which included: detrusor instability (22.2%), rectoenterocele (14.1%), vault prolapse (3.1%), uterine prolapse (1.5%), vesicovaginal fistula (0.8%), dyspareunia (3.9%), recurrent USI (6.2%), late voiding difficulties (3.9%), and recurrent UTIs (4.7%). Other studies have reported similar complications – again, complications which are well known to occur with any SUI surgery – such as the Demirci 2001 study reporting long-term post-operative groin or suprapubic pain (6.8%) and dyspareunia (2.7%); urinary tract injuries (0%) reported by Stevenson 1999; significant wound complications, bleeding, and damage to the ureter, bladder, and urethra reported by Stanton 1985; and high rates of post-operative voiding dysfunction reported by Galloway 1987, Lose 1987, Erikssen 1990, and Parnell 1984. .

Autologous Fascial Slings:

Blaivas explained that one of the reasons that the autologous fascial sling for the treatment of SUI "has never achieved widespread popularity" is because "the complication rate, particularly in the hands of inexperienced surgeons, is probably much higher than that reported in the literature." Further, "[t]he complications are primarily related to placing too much tension on the sling at operation," which "results in either urinary retention of refractory detrusor instability." [Blaivas 1991, Pubovaginal Fascial Sling for the Treatment of Complicated Stress Urinary Incontinence]. Chaikin and colleagues published de novo (3%) or persistent (23%) urge incontinence and permanent urinary retention (2%) in a series of patients after autologous fascial sling repair for SUI. Other complications described in the study include: bladder injury during surgery, urethral injury, prolonged pain, and death. The reported cure rate was 73%, with 19% improved.

Suburethral Slings with Synthetic Mesh:

The perceived disadvantages of the autologous fascial sling procedure "include its technical difficulty, problems with postoperative urinary retention, incisional pain from the fascial harvest site, and the requirement for postoperative hospitalization." [Clemens 2000]. As a result, new techniques using synthetic mesh slings were developed in order to minimize the disadvantages of the autologous sling, such as the incisional pain and technical difficulty. While synthetic slings offered the benefits of "smaller incisions, less postoperative pain, and decreased hospitalization," they may be associated with unique complications as well, such as urogenital tract erosions which "may occur whenever synthetic materials are used." [Clemens 2000]. While the exact etiology of these erosions is unknown, contributing factors include: "the placement of the sling in a plane too close to the urethra, inadequate vaginal tissue coverage, infection, and poor tissue vascularity." The

risk of erosions occurring years after the surgery was not an unknown risk, as Clemens published that "[t]hese erosions may occur many years after sling placement," and that it is essential for urologists who use synthetic materials to be familiar with the diagnosis and treatment of this complication.

While synthetic slings are more commonly associated with the risk of graft erosion or exposure, the autologous sling using a patient's own tissues is also susceptible to such risks. For example, in 2000, Clemens, DeLancey, McGuire et al. concluded that "[p]ersistent painful or irritative symptoms after pubovaginal sling placement may be due to urogenital tract erosion, especially if synthetic materials were used." [Clemens 2000]. Clemens reported 6 vaginal erosions, 6 urethral and vaginal erosions, and 2 bladder erosions, with a mean time from sling placement to treatment of 11.2 months. All symptoms resolved after removal of the eroded sling component. Clemens described how the risk of erosion is "a known but uncommon complication after pubovaginal sling placement," with an incidence range from 0.3% to 23%, noting "lower rates with the use of autologous materials." Clemens also described the importance "for urologists who perform pubovaginal slings to know how to identify and treat sling erosions when they occur." Erosion was defined the Clemens study by "the presence of a foreign material (sutures, sling material, bone anchors) within the urogenital tract."

Iglesia 1997 provides a helpful overview of the complication rates published in the medical literature during the time when surgeons began looking for more durable and less invasive surgical procedures to treat SUI.

Surgeons began using a variety of meshes in gynecologic surgery well before TVT was on the market. [Moore 1995, Lane 1962, Moir 1968, Morgan 1970, Nichols 1973, Stanton 1985, Horbach 1988, and Young 1995].

Table 3A. Suburethral sling with Mersilene mesh: surgical outcome [24–27,64,69,71,75]

Author	No. pts	Follow-up	Cure rate SUI*	Mesh-related complications
Williams 1962 (Mersilene ribbon)	12	Not stated	83% subjective	1 removal for suprapubic abscess
Ridley 1966 (Mersilene ribbon)	17	6 mos	94% subjective	1 bladder erosion 1 urethral erosion 1 graft infection
Nichols 1973	22	1–2 yrs	95% subjective	not reported
Kersey 1983	105	6 mos-5 yrs	84% subjective	2 VVF‡; 3 vaginal erosions with trimming
Iosif 1985	44	3–11 yrs	73% subjective 73% objective	7 sling divisions for retention 2 abscesses
Kersey 1988	100	6 mos–5 yrs	78% subjective	2 Prolene suture exposures
Guner 1994	24	24 mos	96% subjective	none reported
Young 1995	110	13 mos	95% subjective 93% objective	3 voiding dysfuncion 1 midvaginal band 2 vaginal erosions 1 groin sinus

TVT / Midurethral Slings:

The procedures using the paraurethral connective tissues directly (both for plication and/or suspension) for support resulted in prolonged catheterizations from postoperative inability to void from the surgical trauma to the urethra and bladder neck. The retropubic procedures involved surgery in the retropubic space of Retzius with the potential for large blood losses from the dissections near and on the varicose veins in this space, as the surgeon dissects down towards the pubocervical fascia next to the urethra. Brisk bleeding in the space of Retzius was handled with firm vaginal packing for 24 hours. The TVT product applications, when properly performed, largely avoid these varicosities, and have minimal effect on the sensitive paraurethral tissues. Most patients urinated well within hours of the TVT procedure and went home without a foley catheter. The TVT products give my patients the best postoperative results with the least disruption of urinary function.

There are two main ways of carrying out these operations, either by inserting a tape behind the pubic bone through the abdomen ('retropubic'), or through the groin ('transobturator'). [Ford 2015]. TVT offers advantages over conventional repairs in that it is quick and can be done under local anesthesia. [Karram 2003]. Another benefit of TVT and midurethral slings over autologous fascial slings is the significantly shorter operating time and length of stay, as well as fewer perioperative complications and less detrusor overactivity. [Ford 2015].

The Ford 2015 Cochrane Review summarized the adverse effects of midurethral slings as follows: "Tapes passing behind the pubic bone (retropubic) seem to carry a greater risk of injuring the bladder during the operation and of women experiencing problems emptying their bladder completely after surgery. However, this operation leads to less groin pain in the short term. There is some limited evidence that this way of inserting the tape has a lower risk of requiring a repeat operation in the long term compared to tapes passing through the groin (transobturator). There is moderate quality evidence that overall reported rates of tape-related complications are low, such as erosion of the tape into the vagina at about 2% for both routes of tape insertion. The reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of these tapes."

The Ford 2015 Cochrane Review describes how "Major complications such as nerve, bowel or major vascular injuries, pelvic haematoma, necrotizing fasciitis, ischiorectal abscess, and death are uncommon," although they might show up in registries. National registries tracking retropbubic TVT complications reported the following complications: Bladder perforation occurred in 2.7% to 3.9% of cases; Reoperation rates relating to tape insertion or postoperative voiding dysfunction (POVD) ranged from 1.6% to 2.4%; Urinary retention rate was 1.6%; Pelvic haematoma occurred in 0.7% to 1.9% of women; Infection rate was 0.7%; Vaginal tape erosion/extrusion rate was 1.5%; Groin pain occurred in 0.4% of women. [Collinet 2008, Dyrkorn 2010, Kuuva 2002, Koops 2005, Tamussino 2001, Tamussino 2007, and Tincello 2007].

Graft Properties:

It is the surgeon's responsibility to obtain knowledge on new devices and surgical instruments without relying on manufacturers to educate them. [Matthews 2009]. Surgeons like myself are familiar with, and expected to know, the specific mesh properties of the devices they offer to patients, including the pore size, tensile strength, and durability of the TVT mesh.

The Ford 2015 Cochrane Review reinforces the relevancy of the Amid classification as the industry standard for ideal mesh properties. Amid Type 1 meshes have "the highest biocompatibility with the least propensity for infection." [Ford 2015]. Amid Type 1 meshes are have sufficient pore sizes (greater than 75 μm), which helps with tissue integration by easily allowing macrophages, leukocytes, fibroblasts, blood vessels and collagen to transverse the pores, thus promoting "tissue host ingrowth with resultant biocompatibility and low risk of infection (Amid 1997)." [Ford 2015]. As such, the "Amid Type 1 polypropylene, macroporous, monofilament tapes are widely available and now predominate in current clinical practice," and have the best mechanical performance and best tissue integration. [Ford 2015, Boukerrou 2007]. The 2011 Ogah Cochrane Review found that "Monofilament tapes had significantly higher objective cure rates compared to multifilament tapes and fewer tape erosions." [Ogah 2011].

There are multiple studies confirming that TVT mesh does not shrink in the short-term, or in the long-term. [Dietz 2003, Lo 2004, Nilsson 2013, Lukacz 2003, Coda 2003].

Well-Known Complications with All Surgeries to Treat SUI:

Karram and colleagues published in 2003 on complications associated with their first 350 TVT procedures, of which 82% were improved or cured. [Karram 2003, ACOG]. Their published complication rates included: bladder perforation (4.9%), significant bleeding (0.9%), voiding dysfunction (12%), recurrent urinary tract infections (10.9%), erosion or poor healing (0.9%), hematoma (1.7%), nerve injury (0.9%), sling takedown procedure for voiding dysfunction (1.7%), recurrent stress incontinence (2 out of 6 patients who had a takedown), and underwent another procedure for recurrent or persistent incontinence (0.5%). Karram (2003) noted that "Postoperative voiding dysfunction can occur after any operation for stress incontinence," and found that the cutting procedures for the sling takedowns for the patients with prolonged voiding dysfunction were all "easily performed" in less than 20 minutes. Karram concluded that the "TVT has been a very efficacious procedure in our hands. We feel it is safe when performed by surgeons experienced in transvaginal and retropubic anti-incontinence procedures."

The AUA Guidelines updated in 2012 list a numerous well-known operative complications of any incontinence procedure. Subjective complications, such as pain, sexual dysfunction, and voiding dysfunction were reported for synthetic midurethral slings at a frequency of

1%, 0%, and 2%, respectively. By contrast, the AUA reported 6% pain, 3% sexual dysfunction, and 10% voiding dysfunction for the Burch colposuspension, and 10% pain, 8% sexual dysfunction, and an undetermined rate for voiding dysfunction for autologous fascial slings. [AUA Guidelines 2012, Appendix]. The Schimpf 2014 SGS Systematic Review and Novara 2008 Cochrane Review also provide reliable comparative complication rates.

In 2013, the FDA published the review of its results from medical device reports and determined that "The most common complications reported through MDRs for surgical mesh slings for SUI repair, in descending order of frequency, include: pain, mesh erosion through the vagina (also called exposure, extrusion or protrusion), infection, urinary problems, recurrent incontinence, pain during sexual intercourse (dyspareunia), bleeding, organ perforation, neuro-muscular problems and vaginal scarring. Many of these complications require additional medical intervention, and sometimes require surgical treatment and/or hospitalization. With the exception of mesh erosion, the above complications can occur following a non-mesh surgical repair for SUI." [FDA 2013 Considerations about Surgical Mesh for SUI]. This further demonstrates the commonality of the set of complications shared by all pelvic floor surgeries that pelvic floor surgeons would be expected to know. Here is what the FDA had to say about the "unique" risk of mesh erosion or exposure: "The use of mesh slings in transvaginal SUI repair introduces a risk not present in traditional non-mesh surgery for SUI repair, which is mesh erosion, also known as extrusion." The FDA also noted that: "Erosion of mesh slings through the vagina is the most commonly reported mesh-specific complication from SUI surgeries with mesh. The average reported rate of mesh erosion at one year following SUI surgery with mesh is approximately 2 percent. Mesh erosion is sometimes treated successfully with vaginal cream or an office procedure where the exposed piece of mesh is cut. In some cases of mesh erosion, it may be necessary to return to the operating room to remove part or all of the mesh." [FDA 2013 Considerations].

In fact, surgeons were put on notice by the FDA in 2008 of complications associated with POP and SUI mesh devices. The FDA's 2008 Public Health Notification, which applied to SUI and POP mesh devices, warned surgeons that: "The most frequent complications included erosion through vaginal epithelium, infection, pain, urinary problems, and recurrence of prolapse and/or incontinence. There were also reports of bowel, bladder, and blood vessel perforation during insertion. In some cases, vaginal scarring and mesh erosion led to a significant decrease in patient quality of life due to discomfort and pain, including dyspareunia." It's important to note that a complication does not mean that the mesh was defective. By the same logic, the FDA told surgeons in 2008 that "Specific characteristics of patients at increased risk for complications have not been determined. Contributing factors may include the overall health of the patient, the mesh material, the size and shape of the mesh, the surgical technique used, concomitant procedures undertaken (e.g. hysterectomy), and possibly estrogen status."

As of October 20, 2008, the FDA was recommending to physicians performing SUI surgeries that they should:

- "Obtain specialized training for each mesh placement technique, and be aware of its risks.
- Be vigilant for potential adverse events from the mesh, especially erosion and infection.
- Watch for complications associated with the tools used in transvaginal placement, especially bowel, bladder and blood vessel perforations.
- Inform patients that implantation of surgical mesh is permanent, and that some complications associated with the implanted mesh may require additional surgery that may or may not correct the complication.
- Inform patients about the potential for serious complications and their effect on quality of life, including pain during sexual intercourse, scarring, and narrowing of the vaginal wall (in POP repair).
- Provide patients with a written copy of the patient labeling from the surgical mesh manufacturer, if available."

The American Urological Association issued a position statement in 2011, noting the shared complications between synthetic midurethral slings and traditional SUI surgeries: "Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well."

Safety of TVT and Midurethral Slings:

Evidence-based medicine allows surgeons to make clinical decisions based on the highest level of evidence, such as meta-analyses, systematic reviews, and randomized controlled trials. The 2015 Cochrane Review by Ford et al. is one of the most comprehensive and unbiased reviews of the medical literature evaluating the safety and efficacy of synthetic midurethral slings from 81 trials evaluating 12,113 women. [Ford 2015 Cochrane Review]. Some of the findings from the 2015 Cochrane Review found that a retropubic bottom-to-top route (TVT) was more effective than top-to-bottom route (SPARC) for subjective cure, as well as incurring "significantly less voiding dysfunction, and led to fewer bladder perforations and vaginal tape erosions." The author's conclusion was that:

> "Mid-urethral sling operations have been the most extensively researched surgical treatment for stress urinary incontinence (SUI) in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life of women with SUI. With the exception of groin pain, fewer adverse events occur with employment of a transobturator approach. When comparing transobturator techniques of a medial-to-lateral versus a lateral-to-medial insertion, there is no evidence to support the use of one approach over the other. However, a bottom-to-top route was more effective than top-to-bottom route for retropubic tapes."

The 2011 Ogah Cochrane Review evaluated 62 trials involving 7,101 women and found that "Minimally invasive synthetic suburethral sling operations appeared to be as effective as traditional suburethral slings, but with shorter operating time and less postoperative voiding dysfunction and de novo urgency symptoms." Likewise, "Minimally invasive synthetic suburethral sling operations appeared to be as effective as open retropubic colposuspension with fewer perioperative complications, less postoperative voiding dysfunction, shorter operative time, and hospital stay but significantly more bladder perforations. [Ogah 2011].

A study comparing TVT to TVT-Exact showed no statistically significant difference in objective cure (80% for TVT-Exact; 82% for TVT), postoperative pain on the VAS scale, vaginal mesh exposures (0% for both), frequency of tape release (6% for TVT-Exact; 2% for TVT) or tape cut or removed (2% for TVT-Exact; 0% for TVT). [Thubert 2016, European Journal of Obstetrics and Reproductive Biology].

In their 2014 report, the MHRA concluded that from the review of the information available, there appeared to be no evidence that vaginal mesh implants for SUI are unsafe, nor was there evidence to justify MHRA taking enforcement action to take them off the market, or remove them from use.

Synthetic midurethral slings, such as TVT, are the gold standard treatment option for the primary treatment of SUI due to the impressive body of clinical data supporting their safety and efficacy as well as their superiority over traditional surgeries. [Ford 2015, Schimpf 2014, Cox 2013, Tommaselli 2015, Ogah 2011].

The FDA in 2013 stated that "The safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year." [FDA 2013 Considerations].

The leading professional societies and organizations from the United States and across the globe have issued position statements, guidelines, practice bulletins, and results from systematic reviews confirming and endorsing TVT and synthetic midurethral slings as the gold standard surgical repair for SUI based on strong clinical data confirming its safety profile and benefits. [AUGS, SUFU, ACOG, AUA, IUGA, EAU, ICS, NICE, FDA, MHRA, SCENIHR].

I agree entirely with the AUGS-SUFU 2014 Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence that: "The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence. The procedure is safe, effective, and has improved the quality of life for millions of women."

> **Polypropylene material is safe and effective as a surgical implant.**
> "Polypropylene material has been used in most surgical specialties (including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology, and urology) for over five decades, in millions of

patients in the US and the world (personal communication with manufacturers of polypropylene suture and mesh). As an isolated thread, polypropylene is a widely used and durable suture material employed in a broad range of sizes and applications. As a knitted material, polypropylene mesh is the consensus graft material for augmenting hernia repairs in a number of areas in the human body and has significantly and favorably impacted the field of hernia surgery. [6, 7] As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years [8]."

The monofilament polypropylene mesh MUS is the most extensively studied antiincontinence procedure in history.

"A broad evidence base including high quality scientific papers in medical journals in the US and the world supports the use of the MUS as a treatment for SUI [9]. There are greater than 2000 publications in the scientific literature describing the MUS in the treatment of SUI. These studies include the highest level of scientific evidence in the peer reviewed scientific literature [9]. The MUS has been studied in virtually all types of patients, with and without comorbidities, and all types of SUI. Multiple randomized, controlled trials comparing types of MUS procedures, as well as comparing the MUS to other established non-mesh SUI procedures, have consistently demonstrated its clinical effectiveness [9-12] and patient satisfaction [12]. Among historical SUI procedures, the MUS has been studied as long in follow-up after implantation as any other procedure and has demonstrated superior safety and efficacy [8]. No other surgical treatment for SUI before or since has been subject to such extensive investigation."

Polypropylene mesh midurethral slings are the standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients.

"Since the publication of numerous level one randomized comparative trials, the MUS has become the most common surgical procedure for the treatment of SUI in the US and the developed world. This procedure has essentially replaced open and transvaginal suspension surgeries for uncomplicated SUI. There have been over 100 surgical procedures developed for the management of SUI and there is now adequate evidence that the MUS is associated with less pain, shorter hospitalization, faster return to usual activities, and reduced costs as compared to historic options that have been used to treat SUI over the past century. Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard for stress incontinence surgery [13]. Over 3 million MUS have been placed worldwide and a recent survey indicates that these procedures are used by > 99% of AUGS members [14]."

Conclusion

"The polypropylene midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly. With its acknowledged safety and efficacy it has created an environment for a much larger number of women to have access to treatment. In the past, concerns over failure and invasiveness of surgery caused a substantial percent of incontinent women to live without treatment. One of the unintended consequences of this polypropylene mesh controversy has been to keep women from receiving any treatment for SUI. This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence.

Likewise, I agree entirely with the ACOG-AUGS 2015 Practice Bulletin on Urinary Incontinence in Women, which found that:

1. "Synthetic midurethral slings demonstrate efficacy that is similar to traditional suburethral fascial slings, open colposuspension, and laparoscopic colposuspension. Compared with suburethral fascial slings, fewer adverse events have been reported with synthetic midurethral slings. Voiding dysfunction is more common with open colposuspension than with synthetic midurethral slings; and

2. There are substantial safety and efficacy data that support the role of synthetic mesh midurethral slings as a primary surgical treatment option for stress urinary incontinence in women."

Furthermore, I agree entirely with the AUA's Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence that:

1. "Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well; and

2. Multiple case series and randomized controlled trials attest to the efficacy of synthetic polypropylene mesh slings at 5-10 years. This efficacy is equivalent or superior to other surgical techniques. There is no significant increase in adverse events observed over this period of follow-up."

The International Urogynecologic Association wrote a very similar Position Statement on Mid-Urethral Slings for Stress Urinary Incontinence, again, which I fully support:

1. "Mid-urethral slings are minimally invasive procedures developed in Europe in the 1990s to treat female stress urinary incontinence. These slings are narrow, synthetic polypropylene tapes that are surgically placed beneath the middle part of the urethra (water pipe) to provide dynamic support to stop leakage from the bladder. They have been shown to be as effective as more invasive traditional surgery with major advantages of shorter operating and admission times, and a quicker return to normal activities together with lower rates of complications.3 This has resulted in MUS becoming the operation of choice in Europe, Asia, South America, South Africa, Australasia4 and North America5 for treatment of SUI with several million procedures performed worldwide."

Long-Term Studies:

Several long-term observational studies have confirmed the long-term efficacy and safety of TVT at 8 to 17 year follow-up. [Aigmueller 2011, Athanasiou 2014, Heinonen 2013, Nilsson 2013, Serati 2012; Serati 2013, Svenningsen 2013, Groutz 2011, Olsson 2010, Liapis 2008, Nilsson 2013, Tammusinno 2015). Additionally, several well-designed RCTs have demonstrated the superiority of TVT's benefit-risk profile compared to traditional surgeries, such as the 5-year Ward, Hilton RCT, the 5-year TOMUS trial, and the 5-year SISTEr trial.

IFU, Professional Education, and Patient Brochures:

I have reviewed the TVT IFUs, TVT Professional Education materials (Slide Decks, DVDs, TVT Surgeon's Resource Monograph), and the TVT Patient Brochures. Ethicon compiled and distributed to surgeons the TVT Surgeon's Resource Monograph, which was a compilation report from the June 2000 Summit meeting distilling the experience of a 17-surgeon panel and representing more than 1,200 cases. [Eth.Mesh.10027307]. The TVT Monograph included sections on patient selection, preparation, anesthesia, incisions, tension-free placement, post-operative care, precautions, adverse reactions, contraindications, and complications. The monograph discusses the following complications in detail: vaginal healing, retropubic hematoma, vaginal perforation during surgery, difficulty placing needle, bladder perforation, patient cannot void after the procedure, injured urethra, urethral erosion, mesh protrusion or defective healing, vascular injuries, bowel perforation, de novo urge incontinence, infection of the mesh, urinary tract infection, and TVT device failure. The Monograph provides a detailed guide on how to place the TVT tension-free to prevent over-correction by using an instrument to provide counter traction. As of 2000, the Monograph notes that more than 150,000 procedures had been carried out around the world, with 23 clinical papers involving 1,392 patients showing a cure rate of 89% with an improvement of an additional 5%. The Monograph notes that "All surgical procedures have risks and complications and these

entered here should be seen in the context of the published complications of surgery for genuine stress incontinence (Chalia & Stanton 1999). In the Monograph's discussion of mesh protrusion or defective healing, Ethicon was communicating to surgeons that "Inadequate suturing, premature resumption of intercourse, infection, previous surgery, vaginal atrophy or vaginal injury can all result in mesh exposure. Treatment with antibiotics and estrogen replacement when mesh protrusion is discovered may result in re-epithelialization of the mesh and, if necessary, resuturing the vaginal mucosa. This can be avoided by pre-op estrogen treatment, avoiding perforation of the vaginal mucosa and appropriate closure of the vaginal incision." Ethicon's Monograph also communicated to surgeons the risk of urethral erosion resulting from intra-operative injury or possibly from excessive tension," and discussed treatments, such as excision of the tape.

Because 21 CFR 801.901(c) permits a medical device manufacturer to omit from its labeling "directions, hazards, warnings, and other information [that] are commonly known to practitioners by law to use the device," there is no need to warn of obvious, well-known risks. Therefore, the suggestions made by plaintiffs' experts fail to take into account the commonly known complications among pelvic floor surgeons who are performing SUI surgeries. Further, Ethicon's SOP on Regulatory Labeling takes into account the information that is specific to the device, and does not obligate itself to turn an IFU into a medical textbook to list every possible complication. Plaintiffs' experts' methodology neglects the knowledge pelvic floor surgeons have regarding the risks that are shared across the spectrum of pelvic floor surgeries with and without mesh. Plaintiffs' experts have failed to account for the reliance that pelvic floor surgeons place on their education, training, clinical experience, discussions with colleagues, and review of the medical literature to become informed about the risks of the surgeries they are performing, including the frequency and severity of those risks, and how to appropriately manage complications. Plaintiffs' experts have failed to account for the practice guidelines, committee opinions, FDA statements, learning objectives, guidelines, and curricula, industry standards regarding the adverse reactions listed in other manufacturers' IFUs for similar products around the same timeframe, as well as the professional society position statements.

The IUGA 2010 Guideline from Training in FPMRS requires that trainees be able to perform minimally invasive retropubic and transobturator midurethral slings, as well as procedures to remove mesh and sutures.

The ABOG and ABU Guidelines for Leaning in FPMRS requires the trainee to be able to perform and describe the indications, intra and postoperative complications, and success rates following synthetic retropubic and transobturator slings. Additional requirements include the ability to "Identify, evaluate, and manage complications associated with continence surgery, including... foreign body associated complications." Additionally, the ABOG and ABU Guidelines require competency about: Augmenting surgical materials; Discuss different types of graft materials used in prolapse and incontinence surgery, including graft properties, advantages, and risks associated with each graft; Discuss relevant characteristics (pore size, filament strength, flexibility, tensile strength) of

augmenting surgical materials; and Discuss the level of evidence (success and complications) for the use of augmenting materials for prolapse and incontinence surgery.

Furthermore, the ACGME Program Requirements for Graduate Medical Education in FPMRS states that fellows must not only be able to competently perform surgery for urinary incontinence, including native tissue and synthetic slings, but also must demonstrate competence in their knowledge of the indications, limitations, complications, and techniques for urinary incontinence.

The AUA National Medical Student Curriculum notes the importance of the NIH-funded TOMUS trial comparing retropubic midurethral slings to transobturator midurethral slings.

Further, the AUGS Resident Learning Objectives states that residents must understand the difference between a pubovaginal and minimally invasive mid-urethral sling, and be able to understand and perform a mid-urethral sling, using either a retropubic or transobturator approach. Residents are expected to be able to "discuss risks, benefits, and expected outcomes of nonsurgical and surgical management of SUI." Additionally, the AUGS Resident Guidelines requires that residents: Understand the categories of various graft materials; Understand the vital characteristics of synthetic grafts, such as pore size, mono versus polyfilament, materials type; Understand the relative indications for, and complications associated with each graft; and Understand the management of graft complications, both surgical and non-surgical." Residents are then expected to be familiar with the referenced literature on graft materials, TVT, RCTs, and consensus papers on the surgical management of SUI.

There is no reliable literature applicable to TVT that attaches any clinical significance to claims of alleged particle loss, mechanically cut versus laser cut, degradation, cytotoxicity, roping, fraying, or curling when the TVT is used as intended. I have not had any patient experience a complication related to the aforementioned theoretical risks, nor have I seen them supported by any reliable level 1 evidence in the medical literature. There is no legitimate reason to warn surgeons of hypothetical, unsubstantiated risks that would hypothetically, according to plaintiffs' experts, result in well-known complications such as pain, dyspareunia, and mesh exposure.

Weight and Pore Size:

TVT is an Amid Type 1, macroporous (greater than 75 microns), monofilament, polypropylene mesh with a much small surface area and different application than hernia or prolapse meshes. While there is no defined term for lightweight, TVT is commonly referred to in the gynecologic literature as being a lightweight mesh due to its large pore structure. In fact, Ethicon's TVT mesh pore size of 1,379 microns is the largest pore size out of the synthetic midurethral slings available in the United States. [Moalli 2008]. It is a well-known part of the normal healing process for nonmesh surgeries to result in scarring and tissue contracture, which can occasionally cause temporary or long-term pain and/or dyspareunia.

Mechanical versus Laser Cut:
There is no scientific merit to plaintiffs' experts' hypothesis that the mechanically cut feature of TVT or the TVT laser cut option has any clinical significance or impact on patient safety. I am aware that plaintiffs' experts postulate in TVT mechanically cut cases that alleged particle loss somehow creates an increased inflammatory reaction, which then produces pain; and the "sharp" edges of the mesh cause an increase in mesh erosions and exposures. By contrast, plaintiffs' experts in TVT laser cut cases will then speculate that the laser cut method causes an increase in the very same complications (pain, dyspareunia, and mesh erosions/exposures); however, just by a different mechanism (e.g., the way the mesh is cut). In laser cut TVT cases, their experts speculate that the laser cutting method makes the TVT mesh stiffer, which then increases the risk of pain, dyspareunia, and mesh erosion/exposure. These theories fail scientific reliability and are misleading and speculative at best. My clinical experience, discussions with colleagues, and review of the medical literature have not revealed any clinical significance to the method of cutting, nor would I expect any.

Mesh alternatives – Larger pore, lighter weight mesh:
There is no reliable scientific evidence, such as an RCT, comparing a larger-pore/lighter-weight mesh to TVT mesh for the treatment of SUI at the midurethra. I am aware of the Okulu (2013) study comparing Gynemesh PS, Vypro, and Ultrapro used as hand-fashioned pubovaginal slings at the bladder neck, but this study is not comparable to the TVT procedure, nor does it provide any insight as to the comparative nature of Ultrapro vs. TVT. No significance can be attached to the Okulu study given it's extreme deviations in technique, lack of uniformity regarding the size of the mesh implants, small number of patients enrolled, lack of long-term follow-up, and anchoring of the sling rather than placing it tension-free.

Adverse Tissue Response / Chronic Inflammation:
The tissue reaction associated with polypropylene, Prolene sutures, Prolene mesh, and TVT are well documented in the medical literature, the FDA's 1990 down-classification of polypropylene sutures from class III to class II, and Ethicon's pre-clinical testing. The FDA determined in 1990 that "record data show that nonabsorbable polypropylene surgical suture's performance parameters are well documented and understood, and that the generic type of device presents a reasonably uniform risk/benefit profile." The FDA further noted that nonabsorbable polypropylene sutures elicited a milder response than absorbable sutures, and that "[r]ecord data show that nonabsorbable polypropylene suture elicits a very mild chronic inflammatory reaction." "The chronic tissue inflammatory response to nonabsorbable polypropylene surgical suture is observed to be mild, and less than that elicited by certain other sutures." The FDA continued to describe the favorable biocompatibility of polypropylene sutures, stating, "the foreign body response to nonabsorbable polypropylene surgical suture is mild in nature and, therefore, the suture in some circumstances may be preferred to other nonabsorbable sutures." Falconer (2001) examined the histology of 16 women who were operated on with TVT, Mersilene sling, and Prolene. "A minimal inflammatory reaction without a significant change in collagen solubility was found in the Prolene group. In the control group no inflammatory reaction was seen. Mersilene gave rise to a significant foreign body reaction in the paraurethral

connective tissue after surgery. Such a reaction was not found with Prolene." The authors note how during the development of the TVT procedure, "different sling materials were used, such as Teflon, Gore-Tex, Mersilene, and Marlex," but all of those materials "caused a significant amount of tape rejection. Falconer described how there was "practically no tissue reaction at all seen 2 years after TVT surgery when Prolene mesh was used." They also found that "there was no histological difference between paraurethral connective tissue in biopsies from patients operated on with Prolene tape and in controls 2 years after surgery. By the same token there was no statistical difference in collagen concentration or extractability. The diminutive decrease in both these parameters, as observed in the control group, might be the result of age, compensated for in the Prolene group by a slight stimulation of the fibroblasts by the foreign material. This observation is in agreement with the clinical experience from ~80,000 TVT procedures using Prolene mesh with no tape rejection."

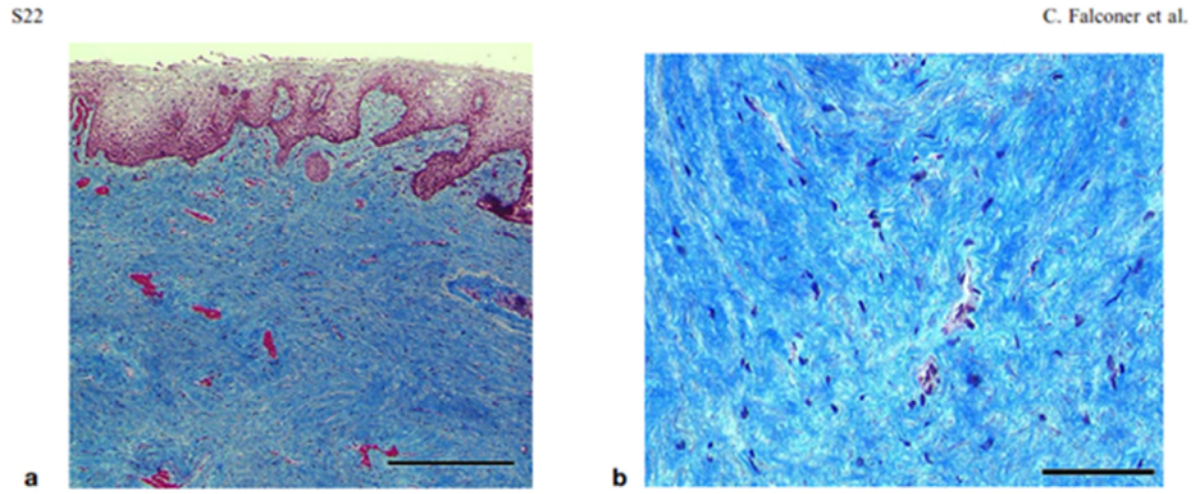

Fig. 3. **a** A specimen from the vaginal wall of a woman with stress incontinence 2 years after Prolene implantation. The squamous epithelium, stained greyish-red, is of a medium height, with some glycogen in the upper cell layers. There is no sign of inflammation in the epithelium. The underlying connective tissue (blue stained) is made up of densely packed collagen bundles. Numerous fibroblasts are seen scattered throughout the connective tissue. Blood vessels of different size are also noted in the connective tissue. There are no signs of fibrosis. Masson's trichrome. Bar = 500 μm. **b** A higher magnification of the same specimen as in **a**. The connective tissue is made up of densely packed collagen bundles. Fibroblasts are scattered throughout the collagen. Some blood vessels are also seen. Masson's trichrome. Bar = 100 μm.

The authors of a pre-clinical study in rabbits comparing the tensile strength, stiffness, and inflammatory reaction of six different sling materials concluded that the "inflammation with the cadaveric fascia and porcine materials may cause rapid clinical deterioration compared with autologous fascia and polypropylene mesh. " They also described how the "fibrosis and scarring noted with polypropylene mesh may also contribute to a more lasting repair." [Krambeck, Elliott, Urology, 2006]. These authors noted their concerns about erosion and infection rates, but they found that "the use of polypropylene mesh has shown promising initial and long-term results similar to that of autologous sling material." The authors results "indicated little degree of inflammation and significant fibrosis, similar to that with autologous material." A rat study by Spiess (2003) evaluating TVT and cadaveric fascia demonstrated "a decrease in tensile strength of cadaveric fascia but not of polypropylene mesh." The authors stated in conclusion that "TVT has morphological and tensile properties that remain well preserved in vivo."

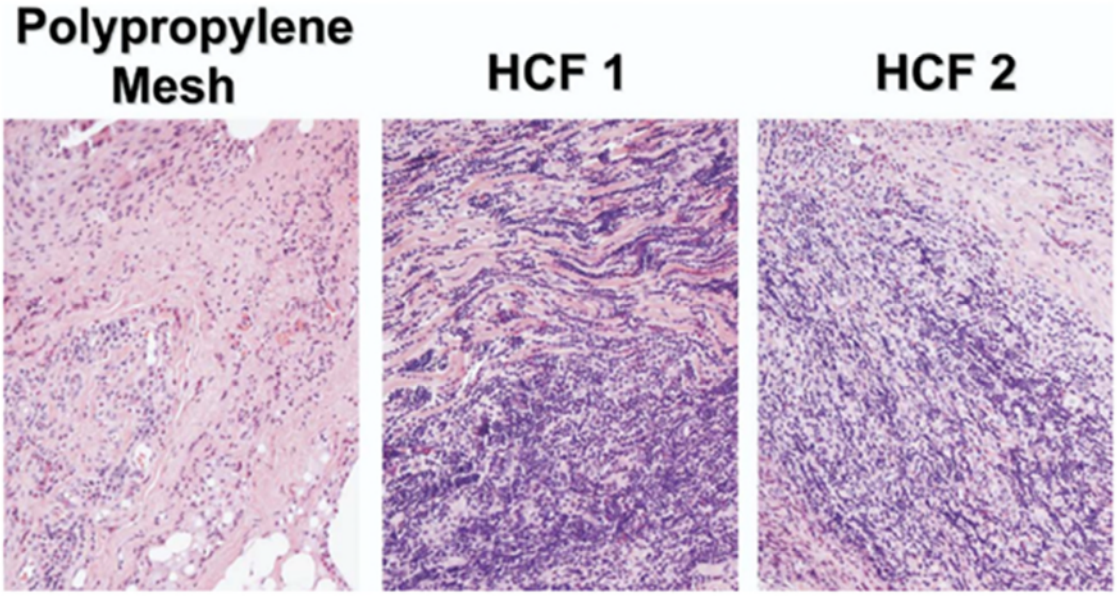

FIGURE 3. *Comparison of degree of inflammation between polypropylene mesh and two types of human cadaveric fascia lata (HCF1 and HCF2) at 12 weeks. High degree of lymphocytes (small round cells) present in human cadaveric fascia compared with mesh.*

Klein-Patel (2011) found no differences in relative inflammatory response when Prolift+M was compared against nonabsorbable Gynemesh.

Hill (2016) demonstrated that the inflammatory reaction for a sling excised for voiding dysfunction demonstrates elevated levels of inflammation compared to mesh that is excised for pain and/or exposure.

Kelly (IUJ, 2016) recently published a review titled, "In vivo response to polypropylene following implantation in animal models: a review of biocompatibility," which states in the conclusion that "The evidence shows that polypropylene evokes a less inflammatory or similar host response when compared with other materials used in mesh devices." The authors noted that "Any foreign material implanted in the body has the potential to elicit a host response," as well as "All foreign materials are associated with a chronic inflammatory reaction, which is variable depending on specific factors, including patient characteristics. Therefore, implanting foreign materials will never be completely risk free." They also described how "Polypropylene is widely reported to be more biocompatible and has shown to elicit the lowest level of inflammatory response compared with other polymeric materials such as nylon, polyacrylonitrile and polyethylene terepthalate."

Cytotoxicity:
There is no reliable scientific evidence to suggest a causal link to polypropylene and any in vivo adverse reactions due to alleged cytotoxicity. [Eth.Mesh.00349228, Ford 2015].

Infection:
The Ford 2015 Cochrane Review states that, "Type 1 mesh has the highest biocompatibility with the least propensity for infection." TVT and TVT-O are Amid type 1 meshes and have been extensively studied for over 20 years. This same comprehensive review reports an infection rate of less than 1% for both the retropubic and transobturator placement of midurethral tapes. Likewise, the thorough systematic review and meta-analysis of Schimpf (Am J Obstet Gynecol, 2014) reports infection rates (wound) of less than 1%. The FDA's 1990 reclassification of polypropylene sutures also noted that "because the nonabsorbable polypropylene surgical suture presents somewhat of a lesser risk than other sutures to potential infection, it is the suture of choice for infected wounds or contaminated wounds that present a substantial risk of infection."

Cancer/Sarcoma:
There is no reliable scientific evidence to suggest a causal link to polypropylene and cancer. [Moalli 2014, King 2014, McGregor 2000, Witherson 2004, AUGS-SUFU FAQ 2014]. I agree with the AUGS-SUFU Frequently Asked Questions by Providers:

> **Is there scientific evidence that the mesh used in polypropylene mid-urethral slings causes cancer in humans?**
> Tumors related to the implantation of surgical grade polypropylene for mid-urethral slings in humans have never been reported. There is no compelling evidence supporting human malignant transformation related to polypropylene despite the millions of individuals implanted with various forms of this material spanning well over a half century world-wide. The possibility that biomaterial prosthetic devices could cause tumors or promote tumor growth has been the focus of extensive research by both clinicians and biomaterial researchers. [9, 10]. It is known that tumor formation related to biomaterials in animals is largely dependent on the physical, not the chemical configuration of the implant, with smooth large surface areas (discs and thin sheets) being potentially carcinogenic, and irregular disrupted surfaces (e.g. those that contain pores as in meshes) lacking carcinogenicity [10, 11].

Degradation:
There is no reliable scientific basis to suggest that degradation occurs in vivo or that there is any clinical significance to alleged degradation. [Clave 2010, Liebert 1976, Woodruff 2008, De Tayrac 2011, Polypropylene Suture Reclassification letter from FDA in 1990, AUGS-SUFU 2014 Position Statement]. I occasionally have looked at explanted mesh slides with the pathologists at my hospital.. One of the studies that plaintiffs' experts rely on to support their speculation that TVT degrades is a study by Clave, a study which has been used in a misleading way as even the authors concluded, "Several hypotheses concerning the degradation of the PP are described below. None of these, particularly direct oxidation, could be confirmed in this study." [Clave 2010]. In fact, a year later, Dr. DeTayrac found no degradation after properly cleaning the mesh. [De Tayrac 2011]. I agree with the AUGS-SUFU Frequently Asked Questions by Providers, which answered the following questions:

Does the MUS mesh made of polypropylene degrade over time?

Polypropylene is a stable and well-accepted biomaterial with a history of over five decades of use in mesh implants. In recent years, concerns regarding implanted polypropylene degradation have been raised as a result of very high- magnification images that show portions of some explanted synthetic meshes with "cracked" surfaces.[8] These surface changes were further hypothesized to lead to adverse clinical outcomes, though this is not supported by the extensive peer-reviewed literature related to polypropylene mesh repairs. Prospective studies have followed patients with implanted mid-urethral slings for 17 years and show excellent durability and safety of the procedure. [5]

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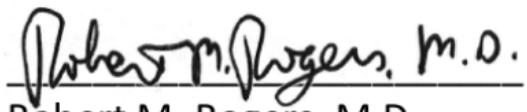

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